Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A composition comprising a hybrid receptor protein-tyrosine kinase selected from:

(i) a cell comprising a hybrid receptor, wherein the hybrid receptor comprises (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said kinase domain being rendered in an active conformation by its association with said Ret extracellular domain,

(ii) a membrane preparation isolated from a cell comprising a hybrid receptor, wherein the hybrid receptor comprises (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said heterologous kinase domain being rendered in an active conformation by its association with said Ret extracellular domain, or

(iii) a hybrid receptor comprising (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said heterologous kinase domain being rendered in an active conformation by its association with said Ret extracellular domain,

wherein the Ret receptor kinase extracellular domain can originate from any species whose genome encodes a Ret receptor kinase,

and wherein the the kinase domain of the heterologous receptor protein-tyrosine kinase can be from any receptor protein-tyrosine kinase of any species.

Claim 2 (previously presented): The composition of claim 1 wherein the kinase domain of the heterologous receptor protein-tyrosine kinase is selected from the kinase domains of EGFR, HER2, HER3, HER4, insulin receptor, IGF-1 receptor, IRR, PDGFR-alpha, PDGFR-beta, CSF-1 receptor, KIT, FLK2, FLK1, FLT4, FGFR1, FGFR2, FGFR3, FGFR4, CCK4, MET (HGF-R), RON, VEGFR1, VEGFR3, TrkA, Eph, AXL, MER, SKY, EphA2, EphA1, EphA3, EphA4, EphA5, EphA6, EphA7, EphA8, EphB1, EphB2, EphB3, EphB4, EphB5, EphB6, RYK, Flt-3, FLT-1, TRKC, TRKA, TRKB, Nck-alpha, Spry, KDR, PDGF-R-alpha, Syk, Blk, FGFR-3, LTK, TIE, Tie2, ROR, DDR1, DDR2, Ret, ROS, LTK, ALK, ROR2, ROR1, RTK106, LMR1, LMR2, LMR3, KLG, RYK, MuSK, LET-23, DAF-2, F59F3.1, F59F3.5, F40G9.13, EGL-15, KIN15, KIN16, TKR-1, C08H9.8, F59F5.3, M01B2.1, R09D1.12, R09D1.13, T01G5.1, T17A3.8, W04G5.6C, W04G5.6N, Y50D4B-4, ZK938.5, B0198.3, F54F7.5, VAB-1, C16B8.1, F11D5.3, C25F6.4, C16D9.2, CAM-1, T10H9.2, B0252.1, F11E6.8, F40A3.5, R151.4, T148.1, T22B11.3, Y38H6C.20, C24G6.2A, F08F1.1, F09A5.2, and F09G2.1.

Claim 3 (previously presented): The composition of claim 2 wherein the kinase domain of the receptor protein-tyrosine kinase is a human tie2 kinase domain.

Claim 4 (previously presented): The composition of claim 1 wherein the modified extracellular domain of the Ret receptor kinase comprises one or more amino acid residue substitutions, deletions or additions that result in one or more unpaired cysteine residues being available for Ret dimer formation.

Claim 5 (withdrawn): The composition of claim 1 wherein the modified extracellular domain of the Ret receptor kinase comprises one or more amino acid residue substitutions at residues selected from Cys 609, Cys611, Cys618, Cys620, Cys630 and Cys634.

Claim 6 (withdrawn): The composition of claim 1 wherein the modified extracellular domain of the Ret receptor kinase comprises one or more amino acid residue substitution selected from C634W, C634R, C634Y, C634F, C634G, C634S, C630F,

C634W, C620F, C618F, C620S, C618S, C620G, C618G, C611G, C611W, C620R, C618R, C609R, C620Y, C618Y, C611Y, and C609Y.

Claim 7 (previously presented): The composition of claim 6 wherein the modified extracellular domain of the Ret receptor kinase comprises the amino acid residue substitution C634W.

Claim 8 (previously presented): The composition of claim 7 wherein the modified extracellular domain of the Ret receptor kinase comprises the extracellular domain of the human Ret receptor kinase with the amino acid residue substitution C634W.

Claim 9 (withdrawn): The composition of claim 1 wherein the modified extracellular domain of the Ret receptor kinase comprises a deletion selected from L633, E632/L633 or residues 592-607.

Claim 10 (previously presented): The composition of claim 1 wherein the hybrid receptor has a transmembrane domain interposed between the modified extracellular domain of the Ret receptor kinase and the kinase domain of the heterologous receptor protein kinase.

Claim 11 (previously presented): The composition of claim 10, wherein the transmembrane domain comprises a transmembrane domain of a Ret receptor kinase.

Claim 12 (previously presented): The composition of claim 1 wherein the composition comprising a hybrid receptor protein-tyrosine kinase is a hybrid receptor comprising (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said heterologous kinase domain being rendered in an active conformation by its association with said Ret extracellular domain.

Claim 13 (withdrawn): A method for detecting a modulator of a selected receptor protein-tyrosine kinase, comprising

(a) providing a hybrid receptor comprising a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and the heterologous kinase domain of the selected receptor protein-tyrosine kinase;

(b) incubating the hybrid receptor with a test sample;

(c) detecting a change in activity of the receptor protein-tyrosine kinase; and

(d) correlating said change with the presence of the modulator in the test sample.

Claim 14 (withdrawn): The method of claim 13 wherein the change in activity of the receptor protein-tyrosine kinase is monitored by autophosphorylation of the hybrid receptor protein kinase, or by its activity on a peptide or protein substrate.

Claim 15 (previously presented): The composition of claim 1 wherein the composition comprising a hybrid receptor protein-tyrosine kinase is a cell comprising a hybrid receptor, wherein the hybrid receptor comprises (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said kinase domain being rendered in an active conformation by its association with said Ret extracellular domain.

Claim 16 (previously presented): The composition of claim 15, wherein the cell is a eukaryotic cell.

Claim 17 (previously presented): The composition of claim 15, wherein the cell is a mammalian cell.

Claim 18 (previously presented): The composition of claim 15, wherein the cell is a human cell.

Claim 19 (previously presented): The composition of claim 15, wherein the cell is an insect cell.

Claim 20 (previously presented): The composition of claim 15, wherein the cell is a yeast cell.

Claim 21 (withdrawn): A method for detecting a modulator of a selected receptor protein-tyrosine kinase, comprising

(a) providing a cell comprising a hybrid receptor, wherein the hybrid receptor comprises a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and the heterologous kinase domain of the selected receptor protein-tyrosine kinase;

(b) incubating the cell with a test sample;

(c) detecting a change in activity of the receptor protein-tyrosine kinase; and

(d) correlating said change with the presence of the modulator in the test sample.

Claim 22 (withdrawn): The method of claim 21 wherein the change in activity of the receptor protein-tyrosine kinase is monitored by autophosphorylation of the hybrid receptor protein kinase, or by its activity on a peptide or protein substrate.

Claim 23: (currently amended): The composition of claim 1 wherein the composition comprising a hybrid receptor protein-tyrosine kinase is a membrane preparation isolated from a cell comprising a hybrid receptor, wherein the hybrid receptor comprises (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor

protein-tyrosine kinase, said heterologous kinase domain being rendered in an active conformation by its association with said Ret extracellular domain[[,]].

Claim 24 (withdrawn): A method for detecting a modulator of a selected receptor protein-tyrosine kinase, comprising

(a) providing a membrane preparation comprising a hybrid receptor, wherein the hybrid receptor comprises a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and the heterologous kinase domain of the selected receptor protein-tyrosine kinase;

(b) incubating the membrane preparation with a test sample;

(c) detecting a change in activity of the receptor protein-tyrosine kinase; and

(d) correlating said change with the presence of the modulator in the test sample.

Claim 25 (withdrawn): The method of claim 24 wherein the change in activity of the receptor protein-tyrosine kinase is monitored by autophosphorylation of the hybrid receptor protein kinase, or by its activity on a peptide or protein substrate.

Claim 26 (currently amended): A nucleic acid encoding a hybrid receptor comprising (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said heterologous kinase domain being rendered in an active conformation by its association with said Ret extracellular domain,
wherein the Ret receptor kinase extracellular domain can originate from any species whose genome encodes a Ret receptor kinase,
and wherein the the kinase domain of the heterologous receptor protein-tyrosine kinase can be from any receptor protein-tyrosine kinase of any species.

Claim 27 (previously presented): The nucleic acid of claim 26, wherein the nucleic acid is DNA.

Claim 28 (previously presented): A vector comprising the nucleic acid of claim 26.

Claim 29 (previously presented): A vector of claim 28 adapted for expression in a cell which vector comprises the regulatory elements necessary for expression of the nucleic acid in the cell operatively linked to the nucleic acid encoding the receptor so as to permit expression thereof.

Claim 30 (previously presented): The vector of claim 28, wherein the vector is a plasmid.

Claim 31 (previously presented): A host cell comprising the vector of claim 28.

Claim 32 (previously presented): The cell of claim 31, wherein the cell is a eukaryotic cell, a mammalian cell, a human cell, an insect cell, a yeast cell, or a prokaryotic cell.

Claim 33 (previously presented): A method for producing a hybrid receptor comprising (a) a modified extracellular domain of the Ret receptor kinase, containing one or more amino acid residue substitutions, deletions or additions that render it capable of activating an intracellular receptor protein-tyrosine kinase domain in a ligand-independent manner, and (b) the kinase domain of a heterologous receptor protein-tyrosine kinase, said heterologous kinase domain being rendered in an active conformation by its association with said Ret extracellular domain, said method comprising growing a host cell comprising the vector of claim 29 under suitable conditions permitting production of said hybrid receptor, and recovering the hybrid receptor.

Claim 34 (previously presented): The method of claim 33, further comprising preparing from the recovered hybrid receptor, a membrane preparation containing the hybrid receptor.

Claim 35 (previously presented): The method of claim 33, further comprising purifying the recovered hybrid receptor.

Claim 36 (new): The composition of claim 1 wherein the Ret receptor kinase extracellular domain originates from human Ret receptor kinase.

Claim 37 (new): The composition of claim 26 wherein the Ret receptor kinase extracellular domain originates from human Ret receptor kinase.